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International application number: PCT/US05/004060

International filing date: 09 February 2005 (09.02.2005)

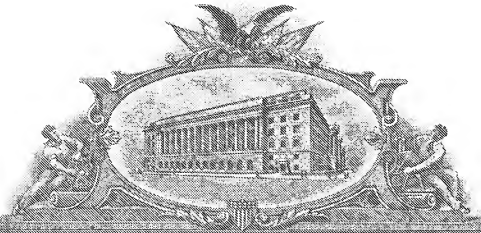
Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 60/542,987
Filing date: 09 February 2004 (09.02.2004)

Date of receipt at the International Bureau: 17 July 2005 (17.07.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)

World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse



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APPLICATION NUMBER: ***60/542,987***
FILING DATE: ***February 09, 2004***
RELATED PCT APPLICATION NUMBER: ***PCT/US05/04060***

Certified by

Jon W. Dudas

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No. EV 362100214 US

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Drew	Pardoll	Brookeville, MD

Additional inventors are being named on the one separately numbered sheets attached hereto

TITLE OF THE INVENTION (500 characters max)

Immune Modulation through Targeting of the NINOR Gene

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

☐ Customer Number:

OR

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☑ Specification *Number of Pages* 5 ☐ CD(s), Number _____

☐ Drawing(s) *Number of Sheets* _____ ☐ Other (specify) _____

☐ Application Data Sheet. See 37 CFR 1.76

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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

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Respectfully submitted,

SIGNATURE _____ Date 09-FEB-04

TYPED or PRINTED NAME Heather A. Bakalyar REGISTRATION NO. 45,282 *(if appropriate)*

TELEPHONE 410-516-8300 Docket Number: 4406

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

PROVISIONAL APPLICATION COVER SHEET
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Docket Number 4406

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Number 2 of 2

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Jason Paradis
Signature

Johns Hopkins University School of Medicine
Office of Technology Licensing

Report of Invention Disclosure Form

This form is to be completed and submitted to the JHU office of Licensing and Technology Development by anyone who believes they have developed a new invention. The purpose of this form is to enable OTL to evaluate whether legal protection to the invention will be sought and/or commercialization pursued. In order for this Report of Invention to be processed by LTD, it must be signed and dated by all inventors, and by the JHU Department Director(s) for all departments involved with the development of this invention. OTL can not process this report until it is complete with all necessary signatures found in Sections A, B and/or C. Visit the LTD web site at http://www.hopkinsmedicine.org/lbd/otl/RptInv.html for HTML and Word 97 downloadable formats of this form.

INVENTION INFORMATION

Title of Invention:
Immune Modulation through Targeting of the MINOR gene

Lead Inventor Information: [the lead inventor is the primary contact person for OTL]

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Are you an HHMI employee or investigator? ☐ Yes ☒ No
Are you a KKI employee or investigator? ☐ Yes ☒ No

Additional inventors: X☐ Yes ☐ No If yes, please complete Additional Inventors section for each inventor.

LTD Internal Use Only: JHU Ref.: 4406 TLA _____ Field of Use _____

ADDITIONAL INVENTOR(S)

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Are you a KKI employee or investigator? ☐ Yes ☒ No

INVENTION DESCRIPTION

Describe the invention completely, using the outline given below.

1. Abstract of the Invention [Briefly describe the invention]

A number of vaccination strategies utilize dendritic cells (DCs) to immunize. While DCs are potent initiators of immune responses, their utility as vaccines may be limited by their relatively short *in vivo* lifespans. We have discovered a new gene in DCs that regulates DC apoptosis and have developed a strategy to inhibit expression of this gene, and by doing so, have shown that we can significantly enhance immune responses. This gene, termed , MINOR, for Mitogen Induced Nuclear Orphan Receptor,is a member of the Nur77 family of apoptosis-inducing genes, and its expression is highly and selectively upregulated in mature DCs, and, our data suggest that it plays a role in natural DC apoptosis. In order to enhance DC survival and function, we have developed a novel approach of inhibiting DC apoptosis via small interfering RNA (**siRNA**) technology. Our data suggest that inhibition of this gene leads to improvement of *ex vivo* DC vaccines and also utilize our system of bone marrow transplantation (**BMT**) with gene modified hematopoietic stem cells (**HSCs**) to analyze its effects on *de novo* generation of DCs *in vivo*.

2. Problem Solved [Describe the problem solved by this invention]

Dendritic cell vaccines have been developed for therapeutic use by generating the DCs both in vivo and in vitro, through various methods. However, these strategies have not been highly effective. Improving vaccination strategies for tumors is a significant goal of immunotherapy. It now appears that DC vaccines can elicit strong immune responses, but they are limited, in part by their short lifespans *in vivo*. While much emphasis has been placed in studying antigen (**Ag**) uptake, processing and presentation as well as costimulatory signal delivery by DCs, little is known about regulation of DC lifespan. Through investigating the unique pattern of gene expression, in DCs, we have identified one whose expression may be at least partly responsible for limiting the efficacy of DC vaccines due to its observed apoptosis-inducing effects. We show that by inhibiting this gene that we can prolong survival of DCs and also enhance immune responses. Thus, this is a novel approach to improving DC vaccines. **(Claims on attached page)**

3. Novelty [Identify those elements of the invention that are new when compared to the current state of the art]

This report describes a new gene that is important for DC function. Expression of the new gene, MINOR, regulates apoptosis in DCs and is likely to be a limiting factor in immunogenicity of these cells. Inhibition of this gene provides a novel means to prolong the immune response in a number of settings. Potentiation of gene expression may also provide a means to inhibit the immune response in order to target hyper or autoimmune type processes.

4. Detailed Description of the invention:

On a separate page(s), attach a detailed description of how to make and use the invention. The description must contain sufficient detail so that one skilled in the same discipline could reproduce the invention. Include the following as necessary:

1- data pertaining to the invention;
2- drawings or photographs illustrating the invention;
3- structural formulae if a chemical;
4- procedural steps if a process
5- a description of any prototype or working model;

In general, a manuscript that has been prepared for submission to a journal will satisfy this requirement.

5. Workable Extent/Scope [Describe the future course of related work, and possible variations of the present invention in terms of the broadest scope expected to be operable; if a ***compound***, describe substitutions, breadth of substituents, derivatives, salts etc., if ***DNA or other biological material***, describe modifications that are expected to be operable, if a ***machine or device***, describe operational parameters of the device or a component thereof, including alternative structures for performing the various functions of the machine or device]

Future plans will center on applying inhibition of this gene in order to enhance immunogenicity in a number of different types of vaccine therapies. In addition, investigation into immunosuppression by potentiating expression of this gene is another therapeutic goal.

2. Problem Solved - continued:

Claims:

1. A new dendritic cell-selective gene, MINOR, capable of inducing apoptosis in dendritic cells
2. Manipulation of MINOR to develop vaccines for cancer through ex vivo DC-based vaccines using molecular targeting, e.g, siRNA.
3. Manipulation of MINOR to develop vaccines for cancer through ex vivo DC-based vaccines using molecular targeting, e.g, signal transduction inhibitors.
4. Manipulation of MINOR to develop vaccines for cancer through ex vivo DC-based vaccines using cell based targeting, e.g, cellular delivery of MINOR targeting molecules.
5. The use of MINOR reagents to classify and/or isolate specific populations of DCs.
6. Manipulation of MINOR to develop vaccines for cancer through blood or marrow transplantation with gene modified cells for transplant, by means of introduction of MINOR inhibiting sequences or genes.
7. Manipulation of MINOR to develop vaccines for cancer through blood or marrow transplantation with cells for transplant treated with MINOR-targeted signal transduction inhibitors or by using cell-based inhibition for delivery to the stem-progenitor cells used for transplant.
8. Manipulation of MINOR by molecular targeting, e.g, siRNA, to develop antigen specific immunity
9. Manipulation of MINOR by molecular targeting, e.g, signal transduction inhibitors, to develop antigen specific immunity.
10. Manipulation of MINOR by cell based targeting, e.g, cellular delivery of MINOR targeting molecules.to develop antigen specific immunity.
11. Manipulation of MINOR to enhance general immunogenicity of cells by cell based targeting, e.g, cellular delivery of MINOR targeting molecules.
12. Manipulation of MINOR to enhance general immunogenicity of cells by gene based approaches for targeting MINOR in immune cells.
13. Manipulation of MINOR to develop vaccines for viral and or bacterial disease for therapy and prophylaxis.
14. Manipulation of MINOR to develop vaccines for immunodeficiencies of unknown origin through inhibition of MINOR to enhance immunogenicity, by siRNA, small molecular weight compounds, or cell based approaches.
15. Manipulation of MINOR in antigen presenting cells by gene or cell-based approaches, to develop novel adjuvants for vaccines for cancers and infectious disease.
16. Potentiation of MINOR as an immunosuppressant for autoimmune or hyperimmune syndromes or to induce tolerance